Tofacitinib, an oral Janus kinase inhibitor, for the treatment of chronic plaque psoriasis: Long-term efficacy and safety results from 2 randomized phase-III studies and 1 open-label long-term extension study

Kim A. Papp, MD, PhD,[a] James G. Krueger, MD, PhD,[b] Steven R. Feldman, MD, PhD,[c] Richard G. Langley, MD,[d] Diamant Thaci, MD,[e] Hideshi Torii, MD, PhD,[f] Stephen Tyring, MD, PhD,[g] Robert Wolk, MD, PhD, DSc,[h] Annie Gardner, MS,[i] Charles Mebus, PhD,[h] Huaming Tan, PhD,[h] Yingchun Luo, PhD,[h] Pankaj Gupta, PhD,[h] Lotus Mallbris, MD, PhD,[j] and Svitlana Tatulych, MD[h]

Waterloo, Ontario, and Halifax, Nova Scotia, Canada; New York, New York; Winston-Salem, North Carolina; Lübeck, Germany; Tokyo, Japan; Houston, Texas; Groton, Connecticut; Cambridge, Massachusetts; and Stockholm, Sweden

Background: Tofacitinib is an oral Janus kinase inhibitor being investigated for psoriasis.

Objectives: We sought to report longer-term tofacitinib efficacy and safety in patients with moderate to severe psoriasis.

Methods: Data from 2 identical phase-III studies, Oral-treatment Psoriasis Trial Pivotal 1 and 2, were pooled with data from these patients in an ongoing open-label long-term extension study. Patients (n = 1861) were randomized 2:2:1 to tofacitinib 5 mg, 10 mg, or placebo twice daily (BID). At week 16, placebo patients were rerandomized to tofacitinib. Pivotal study participants could enroll into the long-term extension where they received tofacitinib at 10 mg BID for 3 months, after which dosing could be 5 or 10 mg BID.

From Probity Medical Research and K. Papp Clinical Research Inc, Waterloo[a]; Rockefeller University, New York[b]; Wake Forest Baptist Health, Winston-Salem[c]; Dalhousie University, Halifax[d]; Comprehensive Center for Inflammation Research, University Hospital Schleswig-Holstein Campus Lübeck[e]; Division of Dermatology, Tokyo Yamate Medical Center[f]; Department of Dermatology, University of Texas Medical School[g]; and Pfizer Inc, Groton,[h] Pfizer Inc, Cambridge,[i] and Dermatology Unit, Department of Medicine Solna, Karolinska Institutet and Karolinska University Hospital, Stockholm.[j]

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Reprint requests: Svitlana Tatulych, MD, Pfizer Inc, 558 Eastern Point Rd, Groton, CT 06340. E-mail: svitlana.tatulych@pfizer.com.

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Results: At week 28, the proportions of patients randomized to tofacitinib 5 and 10 mg BID achieving 75% or greater reduction in Psoriasis Area and Severity Index score from baseline were 55.6% and 68.8%, and achieving Physician Global Assessment of clear or almost clear were 54.7% and 65.9%. Efficacy was maintained in most patients through 24 months. Serious adverse events and discontinuations because of adverse events were reported in less than 11% of patients over 33 months of tofacitinib exposure.

Limitations: There was no dose comparison beyond week 52.

Conclusions: Oral tofacitinib demonstrated sustained efficacy in patients with psoriasis through 2 years, with 10 mg BID providing greater efficacy than 5 mg BID. No unexpected safety findings were observed. (J Am Acad Dermatol 2016;74:841-50.)

Key words: efficacy; Janus kinase inhibitor; long-term; psoriasis; randomized controlled trial; safety; tofacitinib.

CAPSULE SUMMARY

- Tofacitinib is an oral Janus kinase inhibitor being investigated for psoriasis. Short-term efficacy has previously been demonstrated for moderate to severe psoriasis.
- We show maintenance of tofacitinib efficacy through 2 years, with no unexpected safety findings.
- This supports the continued evaluation of tofacitinib as a potential, long-term, oral treatment option for psoriasis.

Clinical disease control for moderate to severe chronic plaque psoriasis typically requires continuous, long-term treatment.[1] Although several treatment options are available, a substantial proportion of patients with psoriasis are not receiving treatment or are under-treated, because of long-term safety concerns, poor tolerability, failure to achieve or maintain treatment goals, patient preference/tolerability for administration route, cost of medication, and/or access and reimbursement issues.[2-5]

Tofacitinib is an oral Janus kinase inhibitor that is being investigated for psoriasis. Two phase-III studies (Oral-treatment Psoriasis Trial [OPT] Pivotal 1 and 2) have demonstrated efficacy and safety of continuous tofacitinib treatment versus placebo over 16 weeks.[6] Here we report the long-term efficacy and safety of tofacitinib, comprising data from the Pivotal studies pooled with interim data from an ongoing long-term extension (LTE) study that enrolled patients who had participated in the Pivotal studies. Efficacy was compared between tofacitinib dosed 5 or 10 mg twice daily (BID) up to week 28, and maintenance of response was assessed up to 2 years. Long-term safety was assessed as of the interim LTE data cut-off (April 4, 2014).

METHODS

Patients

Patient criteria for the Pivotal studies are described elsewhere.[6] Briefly, patients were aged 18 years or older with a diagnosis of plaque-type psoriasis for 12 months or longer before first study drug dose, had a Psoriasis Area and Severity Index (PASI) score 12 or higher, had Physician Global Assessment (PGA) of moderate or severe (5-point scale: 0 = clear, 4 = severe), and had 10% or more affected body surface area. Key exclusion criteria included recent infections, current malignancy or history of malignancies (except for adequately treated or excised basal/squamous cell carcinoma or cervical carcinoma in situ), and history of untreated or inadequately treated latent or active *Mycobacterium tuberculosis* infection.

Study design

The study designs for OPT Pivotal 1 (NCT01276639) and OPT Pivotal 2 (NCT01309737) are described elsewhere.[6] Both were phase-III, multisite, randomized, double-blind clinical studies. Patients were randomized 2:2:1 to tofacitinib 5 mg, 10 mg, or placebo BID. At week 16, all placebo patients were rerandomized to tofacitinib and followed up to 52 weeks. All patients who participated in a Pivotal study for 12 weeks or longer were eligible for enrollment into the open-label LTE study (NCT01163253). Patients who did not achieve either 75% or greater reduction in PASI score from baseline (PASI75) or a PGA of clear or almost clear (PGA response) at week 28 in the Pivotal studies were protocol-mandated to be withdrawn, with the option to enroll into the LTE study (Fig 1).

Upon LTE study enrollment, all patients received tofacitinib 10 mg BID for 3 months. After 3 months,

Abbreviations used:

AE:	adverse event
BID:	twice daily
CI:	confidence interval
HZ:	herpes zoster
IR:	incidence rate
LTE:	long-term extension
NMSC:	nonmelanoma skin cancer
OPT:	Oral-treatment Psoriasis Trial
PASI:	Psoriasis Area and Severity Index
PASI75:	75% or greater reduction in Psoriasis Area and Severity Index score from baseline
PASI90:	90% or greater reduction in Psoriasis Area and Severity Index score from baseline
PGA:	Physician Global Assessment
SAE:	serious adverse event
UV:	ultraviolet

investigators could adjust dose at each study visit (every 3 months) to tofacitinib 5 or 10 mg BID, based on safety or efficacy.

All studies were conducted in compliance with the Declaration of Helsinki and International Conference on Harmonisation Good Clinical Practice Guidelines and were approved by the institutional review boards and/or independent ethics committees at each investigational center. All patients provided written, informed consent.

Efficacy assessments

Efficacy was assessed at scheduled visits up to 2 years across the Pivotal and LTE studies for all patients who were randomized and treated with tofacitinib in the Pivotal studies, and included the proportion of patients achieving a PGA response; proportion achieving PASI75; proportion achieving 90% or greater reduction in PASI score from baseline (PASI90); and change from baseline in PASI score.

Safety assessments

Adverse events (AEs), serious AEs (SAEs), and discontinuations because of AEs were reported for all patients from the first day of tofacitinib exposure. Safety events of special interest included: serious infections, herpes zoster (HZ), opportunistic infections (including tuberculosis), malignancies (excluding nonmelanoma skin cancer [NMSC]), NMSC, major adverse cardiovascular events (adjudicated by a sponsor-independent, external committee of experts), and gastrointestinal perforations. Clinical laboratory tests, vital sign assessments, physical examinations, and 12-lead electrocardiograms were performed at selected visits.

Statistical analyses

Data were pooled across the 2 Pivotal studies including additional long-term data for these patients from the LTE, using an interim data-cut of April 4, 2014 (study ongoing; database unlocked). Data are reported continuously for each patient, regardless of whether they were in a Pivotal study or continuing in the LTE, and all time points are referenced from the first day of the Pivotal studies.

The efficacy analysis set included all patients who were initially randomized and received 1 or more doses of tofacitinib in a Pivotal study. Efficacy data are reported at visits through 2 years across the Pivotal and LTE studies; the relatively small number of patients after 2 years precluded meaningful analysis beyond this time point. Efficacy data through week 28 are presented by treatment group based on randomization in the Pivotal studies, when most patients were still receiving their initial randomization dose. After week 28 a single group is presented comprising patients receiving all tofacitinib doses. Patients initially randomized to placebo were not included in the efficacy analyses presented. Missing data were handled using last observation carried forward. Maintenance of efficacy was compared by treatment group from weeks 16 to 52 using data pooled from the Pivotal studies (excluding LTE data).

The safety analysis set included all patients who received 1 or more doses of tofacitinib, including those who were rerandomized from placebo to tofacitinib at week 16, and all events are reported through April 4, 2014. For patients who advanced from placebo to tofacitinib a new baseline was established, with the first day of tofacitinib treatment considered day 1. To allow comparison of safety events between tofacitinib doses, data are presented for exposure in the Pivotal studies (weeks 0-52; excluding LTE data) based on received dose.

Data are also reported for total tofacitinib exposure from the first day of exposure in the Pivotal studies through April 2014 in the LTE (33 months), to assess incidence of AEs over the longest exposure period possible. Total tofacitinib exposure data are presented for patients who received tofacitinib 10 mg BID for 80% or more of their study duration (10 mg BID group) and for all pooled patients regardless of tofacitinib dose. Incidence rates (IRs) and 95% confidence intervals (CIs) for safety events of special interest were calculated using person-time data adjusted for exposure (patients with event/100 patient-years).

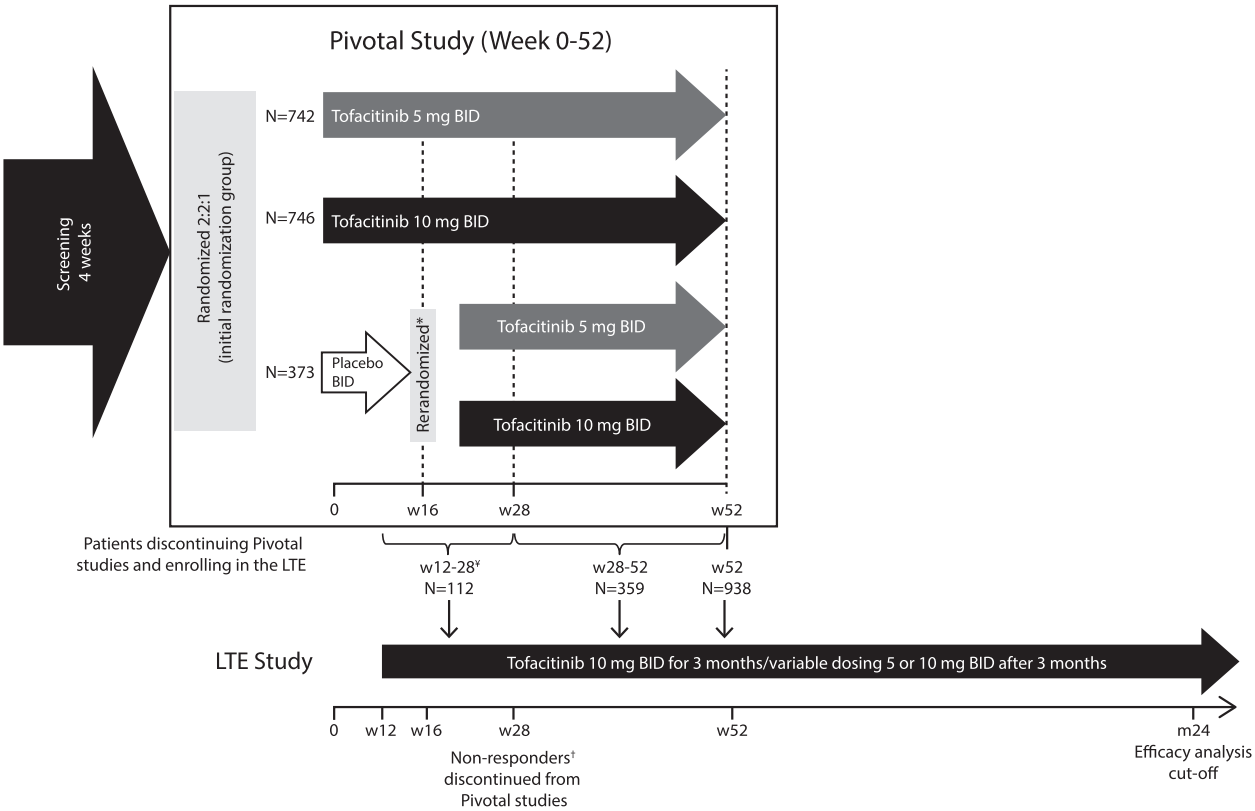

Fig 1. Study design. *Patients included in the safety analysis from first day of exposure; not included in the efficacy analysis. †Patients not achieving ≥75% reduction tofacitinib in Psoriasis Area and Severity Index score from baseline or Physician Global Assessment response at week 28. ¥Three patients deviated from the study protocol and were enrolled into the long-term extension study after <12 weeks participation in a Pivotal study. *BID*, Twice daily; *LTE*, long-term extension; *M*, month; *N*, number; *W*, week.

RESULTS

Patients

In the OPT Pivotal studies 1859 patients were randomized and received treatment. Overall, 1021 (54.9%) patients completed OPT Pivotal 1 or 2 through week 52, 1409 patients enrolled into the LTE study and, at the data-cut, 990 patients were still receiving tofacitinib in the LTE (Figs 1 and 2). Mean total daily dose beyond month 7 (week 28) to month 24 (data presented pooled across doses) was 17.9 mg. Demographics and baseline disease characteristics were similar across treatment groups (Table I).

Efficacy

At week 16, significantly more patients achieved PASI75 and PGA response with tofacitinib 5 and 10 mg BID versus placebo, as previously reported.[6] From week 16 to 28 the proportion of patients achieving PASI75 increased further with both tofacitinib doses; at week 28, a greater proportion of patients initially randomized to tofacitinib 10 mg BID achieved PASI75 versus 5 mg BID (68.8% vs 55.6%, respectively) (Fig 3, *A*). Of patients who achieved PASI75 at week 16 with tofacitinib 5 and 10 mg BID, 74.1% and 79.4%, respectively, maintained response through week 52 in the Pivotal studies (Fig 4, *A*). PASI75 was also maintained in most patients with all tofacitinib doses through month 24 (Fig 3, *A*). Similar patterns of efficacy response and maintenance were observed with PASI90 (Fig 3, *B*, and Fig 4, *B*) and change from baseline in PASI score (Fig 3, *C*).

PGA response rates increased from week 16 to 28 for patients initially randomized to tofacitinib 5 and 10 mg BID, and at week 28 were 54.7% and 65.9%, respectively (Fig 3, *D*). Of patients who achieved a PGA response at week 16 with tofacitinib 5 and 10 mg BID, 62.0% and 71.6%, respectively, maintained their response through week 52 in the Pivotal studies (Fig 4, *C*). PGA responses were maintained in most patients through month 24 (Fig 3, *D*).

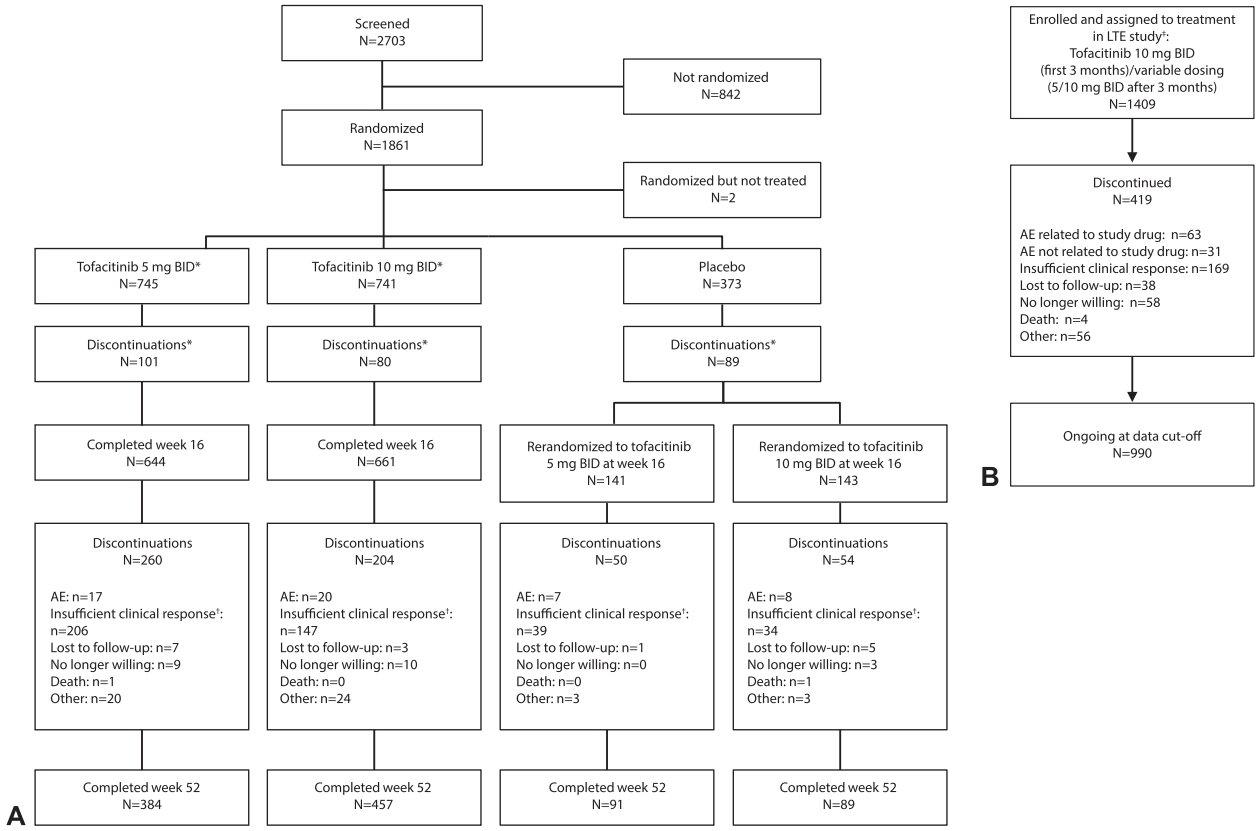

Fig 2. Patient disposition: through week 52 in the Pivotal studies (**A**) and through April 2014 in the long-term extension (LTE) study (**B**). *Causes of discontinuations up to week 16 have previously been reported.[6] †Patients not achieving ≥75% reduction in Psoriasis Area and Severity Index score from baseline or Physician Global Assessment response at week 28 were protocol-mandated to be withdrawn from the study but had the option to enroll into the LTE study at this point. ‡Patients who completed ≥12 weeks in a Pivotal study were eligible to enroll in the LTE study. *AE*, Adverse event; *BID*, twice daily.

Table I. Patient demographics and baseline disease characteristics, according to initially randomized treatment group (full analysis set)

	Tofacitinib 5 mg BID N = 745	Tofacitinib 10 mg BID N = 741	Placebo N = 373
Age,* y (range)	46.0 (18.0-79.0)	45.0 (18.0-82.0)	45.0 (18.0-75.0)
Male, n (%)	529 (71.0)	518 (69.9)	244 (65.4)
Weight,* kg (range)	85.5 (40.8-218.6)	86.0 (38.6-175.0)	86.0 (42.0-188.2)
Race, n (%)			
White	611 (82.0)	610 (82.3)	312 (83.6)
Black	21 (2.8)	17 (2.3)	8 (2.1)
Asian	71 (9.5)	74 (10.0)	33 (8.8)
Other	42 (5.6)	40 (5.4)	20 (5.4)
PASI score* (range)	20.0 (9.5-60.9)	20.0 (12.0-66.0)	19.8 (9.6-54.8)
PGA, n (%)			
Mild	2 (0.3)	1 (0.1)	1 (0.3)
Moderate	635 (85.2)	631 (85.2)	327 (87.7)
Severe	108 (14.5)	109 (14.7)	45 (12.1)

BID, Twice daily; *PASI*, Psoriasis Area and Severity Index; *PGA*, Physician Global Assessment.
*Data are median values.

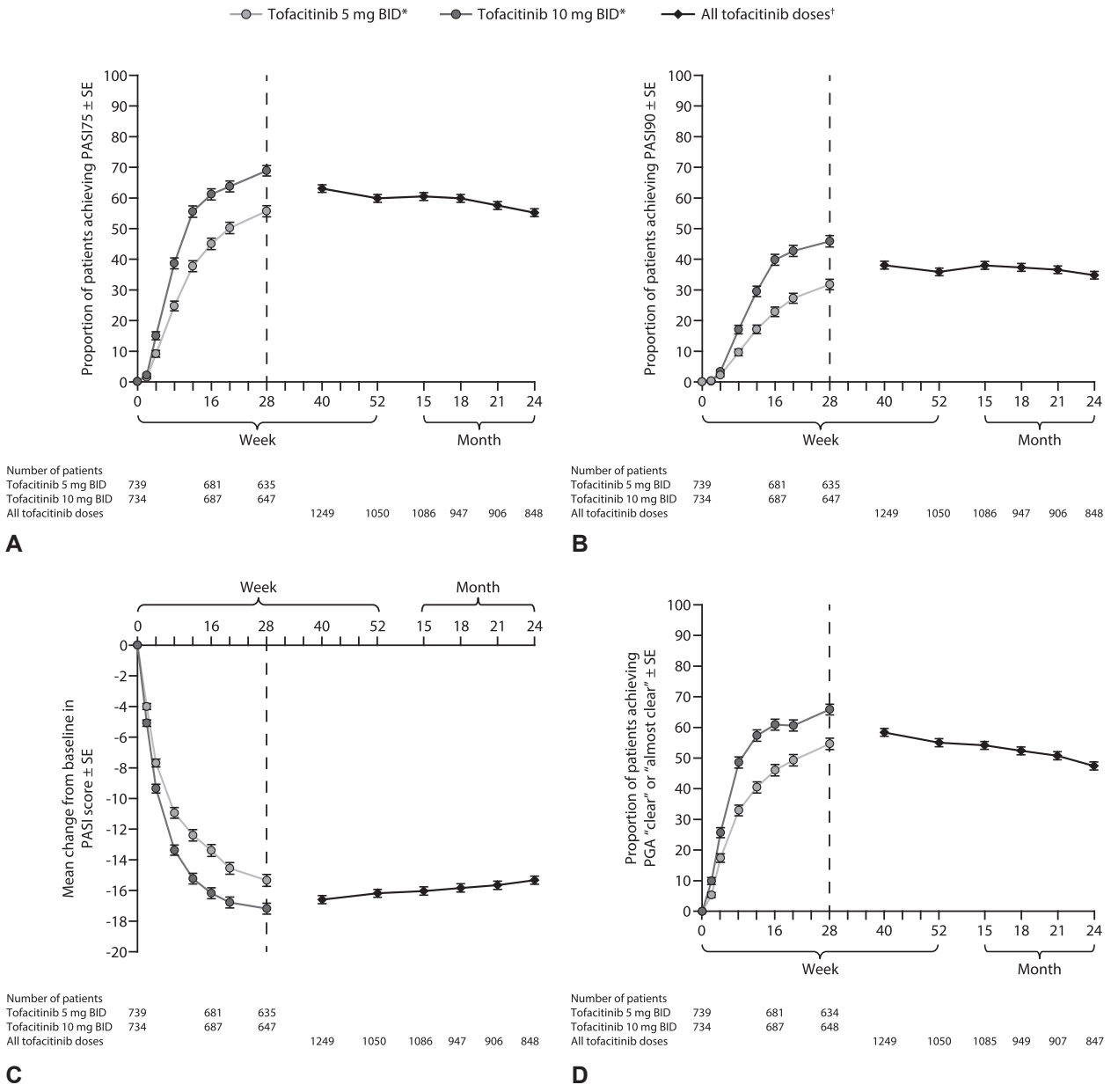

Fig 3. Psoriasis. Proportion of patients achieving: ≥75% (**A**) or ≥90% (**B**) reduction in Psoriasis Area and Severity Index (PASI) score from baseline response. **C**, Change from baseline in PASI score. Physician Global Assessment response of clear or almost clear (full analysis set, last observation carried forward) (**D**). *Treatment groups are presented according to the initially randomized dose at the start of the Pivotal studies. †From week 40 to month 24 data are presented pooled across all tofacitinib doses. Dose comparisons are made through week 28 (*dashed line*). *BID*, Twice daily; *PASI75*, 75% or greater reduction in Psoriasis Area and Severity Index score from baseline; *PASI90*, 90% or greater reduction in Psoriasis Area and Severity Index score from baseline; *PGA*, Physician Global Assessment; *SE*, standard error.

Safety

To allow dose comparisons, safety events through week 52 in the Pivotal studies are reported for 886 (616.6 patient-years) and 884 (660.0 patient-years) patients who received tofacitinib 5 and 10 mg BID, respectively. Rates of SAEs and discontinuations because of AEs were low and similar between tofacitinib doses in the Pivotal studies (<6.0%) (Table II). The most common AEs were nasopharyngitis and upper respiratory tract infection (Table II). Deaths occurred in 4 patients receiving tofacitinib 5 mg BID (esophageal carcinoma,

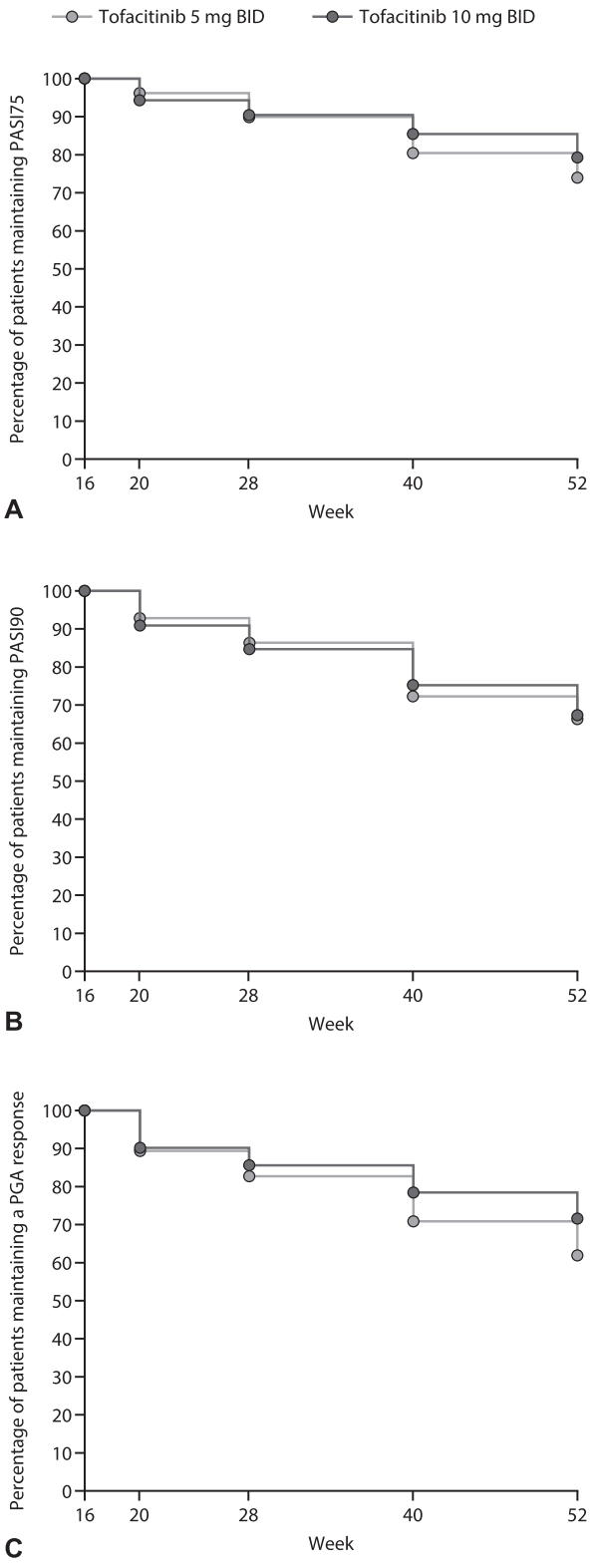

Fig 4. Psoriasis. Proportion of patients maintaining efficacy between week 16 and 52 in the Pivotal studies (among patients with a week 16 response; full analysis set) for: ≥75 (**A**) or ≥90% (**B**) reduction in Psoriasis Area and Severity Index score from baseline response; and Physician Global Assessment response (**C**). *BID*, Twice daily; *PASI75*, 75% or greater reduction in Psoriasis Area and Severity Index score from baseline; *PASI90*, 90% or greater reduction in Psoriasis Area and Severity Index score from baseline; *PGA*, Physician Global Assessment.

malignant lung neoplasm, myocardial infarction [n=2]) and 1 receiving 10 mg BID (cardiac arrest). IRs for safety events of special interest were low for both doses through week 52 (Table II). Although a dose-response was observed for serious infections, HZ and NMSC, the 95% CIs for each IR overlapped and the IR difference was small between dose groups; no dose response was observed for malignancies (excluding NMSC).

Safety events are also reported for the total tofacitinib exposure (first day of tofacitinib exposure in Pivotal studies through April 2014 in the LTE), to describe the longer-term safety profile of tofacitinib. This included data from 1807 patients (2704.8 patient-years) in total (all tofacitinib doses) and 879 patients (1284.7 patient-years) in the tofacitinib 10 mg BID group (10 mg BID for ≥80% of the study duration); 502 patients in total and 237 patients in the 10 mg BID LTE group received tofacitinib for more than 2 years. Over 33 months, 10.1% of patients experienced SAEs and 10.7% of patients discontinued because of AEs (Table II). The most common AEs remained nasopharyngitis and upper respiratory tract infection (Table II). As expected, the number and percentage of reported AEs increased with longer exposure. However, with the exception of HZ, exposure-adjusted IRs for safety events of special interest were comparable between the total tofacitinib exposure and the first 52 weeks (Table II), suggesting no increased risk of these events over time. The IRs for HZ were higher for the total tofacitinib exposure versus the first 52 weeks, although 95% CIs overlapped between time periods. Most HZ cases (59/67 [88.1%]) resolved without complications; 4 cases were classified as SAEs (leading to discontinuation) and 5 cases of postherpetic neuralgia were reported.

A total of 10 (0.6%) deaths (within 30 days of last study drug dose) were reported for the total tofacitinib exposure, with an IR of 0.37 (95% CI 0.18-0.68). Further to the 5 deaths discussed above, causes of death were pancreatic carcinoma, cardiac arrest, acute respiratory death syndrome, road traffic accident, and metastatic lung cancer. One additional death (road traffic accident) occurred with a

Table II. Summary of treatment-emergent adverse events (all cause; safety analysis set)

	Pivotal study wk 0-52*		Total tofacitinib exposure†	
	Tofacitinib 5 mg BID N = 886	Tofacitinib 10 mg BID N = 884	Tofacitinib 10 mg BID‡ N = 879	Tofacitinib all doses N = 1807
Total patient exposure, patient-years	616.63	659.96	1284.69	2704.75
Duration of exposure, d, median (range)	253 (1-393)	345.5 (1-393)	548 (1-1016)	602 (1-1026)
Patients with ≥1 AE, n (%)	567 (64.0)	595 (67.3)	689 (78.4)	1414 (78.3)
AEs leading to discontinuation, n (%)	46 (5.2)	47 (5.3)	99 (11.3)	194 (10.7)
SAEs,§ n (%)	46 (5.2)	48 (5.4)	89 (10.1)	183 (10.1)
Most common AEs, n (%); reported in ≥5% of patients in any group				
Nasopharyngitis	94 (10.6)	116 (13.1)	166 (18.9)	340 (18.8)
Upper respiratory tract infection	66 (7.4)	73 (8.3)	119 (13.5)	227 (12.6)
Blood creatine phosphokinase increased	47 (5.3)	76 (8.6)	106 (12.1)	213 (11.8)
Headache	55 (6.2)	55 (6.2)	70 (8.0)	157 (8.7)
Hypercholesterolemia	42 (4.7)	50 (5.7)	66 (7.5)	126 (7.0)
Arthralgia	29 (3.3)	31 (3.5)	51 (5.8)	107 (5.9)
Urinary tract infection	24 (2.7)	22 (2.5)	42 (4.8)	93 (5.1)
Diarrhea	36 (4.1)	31 (3.5)	39 (4.4)	93 (5.1)
Hyperlipidemia	20 (2.3)	29 (3.3)	45 (5.1)	88 (4.9)
Hypertension	24 (2.7)	21 (2.4)	39 (4.4)	86 (4.8)
Influenza	10 (1.1)	26 (2.9)	48 (5.5)	72 (4.0)
AEs of special interest, n [%], IR (patients with event/100 patient-years; 95% CI)				
Serious infections//	11 [1.2]	18 [2.0]	27 [3.1]	52 [2.9]
	1.78 (0.89-3.19)	2.73 (1.62-4.32)	2.10 (1.39-3.06)	1.93 (1.44-2.53)
Herpes zoster (serious and nonserious)¶	7 [0.8]	13 [1.5]	34 [3.9]	67 [3.7]
	1.14 (0.46-2.35)	1.98 (1.06-3.39)	2.70 (1.87-3.78)	2.53 (1.96-3.21)
Opportunistic infection	2 [0.2]	0 [0.0]	1 [0.1]	8 [0.4]
	0.32 (0.04-1.17)	0.00	0.08 (0.00-0.43)	0.30 (0.13-0.58)
Malignancies (excluding NMSC)	9 [1.0]	4 [0.5]	12 [1.4]	31 [1.7]
	1.46 (0.67-2.77)	0.61 (0.17-1.55)	0.93 (0.48-1.63)	1.15 (0.78-1.63)
NMSC	3 [0.3]	8 [0.9]	13 [1.5]	19 [1.1]
	0.49 (0.10-1.42)	1.22 (0.53-2.40)	1.02 (0.54-1.74)	0.71 (0.43-1.10)
MACE	3 [0.3]	2 [0.2]	5 [0.6]	11 [0.6]
	0.49 (0.10-1.42)	0.30 (0.04-1.09)	0.39 (0.13-0.91)	0.41 (0.20-0.73)
Gastrointestinal perforation	1 [0.1]	0 [0.0]	0 [0.0]	1 [0.1]
	0.16 (0.00-0.90)	0.00	0.00	0.04 (0.00-0.21)

AE, Adverse event; *BID*, twice daily; *CI*, confidence interval; *IR*, incidence rate; *MACE*, major adverse cardiovascular event; *n*, number of patients with event; *N*, number of patients in treatment group; *NMSC*, nonmelanoma skin cancer; *SAE*, serious adverse event.

*Weeks 0-52 includes tofacitinib exposure in the Pivotal studies for patients initially randomized to tofacitinib in the Pivotal studies from week 0-52, and patients who were advanced from placebo to tofacitinib from week 16-52; safety events are reported from the first day of tofacitinib exposure.

†From the first dose of tofacitinib in Oral-treatment Psoriasis Trial Pivotal 1 or 2 or long-term extension, up until the data-cut on April 4, 2014, among subjects enrolled from Oral-treatment Psoriasis Trial Pivotal 1 or 2.

‡For ≥80% of their total tofacitinib exposure.

§AEs that resulted in death, were life-threatening, required hospitalization, resulted in significant disability, or resulted in congenital anomaly/birth defect.

//Any infection (viral, bacterial, and fungal) requiring parenteral antimicrobial therapy or hospitalization, or meeting any other criteria to be classified as an SAE.

¶Serious herpes zoster was reported in 4 (0.2%) patients over the total tofacitinib exposure with all doses.

placebo-treated patient before rerandomization to tofacitinib.

DISCUSSION

Previous reports in patients with moderate to severe plaque psoriasis have shown significantly greater efficacy with short-term (up to 16 weeks) tofacitinib therapy versus placebo[6,7]; this analysis demonstrated maintenance of clinical response for up to 2 years across the Pivotal and LTE studies with continuous tofacitinib treatment. From week 16 to 28 clinical responses increased

further, and tofacitinib 10 mg BID showed greater efficacy versus 5 mg BID (~65% vs 55% of patients achieving PASI75/PGA response). Moreover, most patients who achieved a PASI75 or PGA response at week 16 maintained their response through week 52 in the Pivotal studies. Efficacy was further maintained, with the overall response rate of ~50% for PASI75 and PGA, and ~35% for PASI90 at month 24. The variable long-term dosing in this study reflects real-life practice, with dose changes based on clinical patient treatment in response to efficacy and safety findings.

Current oral treatment options for psoriasis include the traditional systemics: methotrexate, cyclosporin, and acitretin; in addition, the small molecule phosphodiesterase-4 inhibitor apremilast recently became available in the United States and European Union.[8] Efficacy of tofacitinib compares favorably with traditional systemic treatments,[9-13] with 10 mg BID providing greater efficacy compared with methotrexate,[9,12] and acitretin,[11,13] and similar maintenance of response,[9-13] although no head-to-head studies are available to allow direct comparisons. In a study of apremilast 30 mg BID, the proportion of patients achieving PASI75 was appreciably lower (~30%) than reported here with tofacitinib (~60%) over 52 weeks. Efficacy was maintained in a similar proportion of patients with both treatments through week 52; data beyond week 52 are not published for apremilast.[14] In addition, a 12-week phase-III study directly comparing tofacitinib with the biologic therapy etanercept demonstrated noninferiority of tofacitinib 10 mg BID to etanercept with similar incidence of safety events; tofacitinib 5 mg BID did not meet noninferiority criteria versus etanercept.[7] Therefore, tofacitinib may offer a viable alternative to other psoriasis treatments as it appears to be tolerated long-term and to have high initial efficacy, with clinical response maintained over time in most patients.

Safety findings through week 52 were consistent with those previously reported in phase-III studies of tofacitinib for psoriasis with durations of 12 to 56 weeks.[6,7,15] No dose-response was observed for the overall rate of AEs, SAEs, or discontinuations because of AEs through week 52. The rates of SAEs and discontinuations because of AEs over 52 weeks of tofacitinib treatment are similar to that of apremilast in psoriasis, with infections the most common AEs.[14] Unlike conventional oral treatments such as methotrexate and cyclosporine,[8,12] no evidence of end-organ toxicity was observed over time with tofacitinib. Comparison of IRs between the first 52 weeks' exposure and total exposure indicated no increased risk of safety events with increased tofacitinib duration, with the exception of HZ, which had a numerically higher IR for the total exposure. However, most HZ cases resolved without complications, and safety event monitoring over longer tofacitinib exposure is continuing. Increased risk of HZ with tofacitinib treatment has been reported in patients with psoriasis who are Japanese, biologic-experienced, older than 65 years, or have diabetes.[16]

A recently published analysis of the Clalit Health Service database including over 500,000 patient-years of follow-up reported IRs for HZ ranging from 0 to 3.23 events/100 patient-years with various systemic psoriasis treatments.[17] The 95% CIs for tofacitinib overlapped with those of other treatments including psoralen and ultraviolet (UV)A, UVB, cyclosporin, infliximab, and methotrexate or acitretin in combination with biologics.[17] When looking at tofacitinib exposure up to 52 weeks in the Pivotal studies, the IR for HZ with 5 mg BID appeared similar to IRs reported for methotrexate, etanercept, adalimumab, psoralen and UVA, and UVB, and the IR with 10 mg BID appeared similar to cyclosporine, infliximab, and methotrexate or acitretin with biologics.[17]

There are some methodologic limitations inherent to studies assessing the long-term efficacy of treatments, particularly the drop-out of patients over time. The assumption underlying the last observation carried forward handling of missing data values was that efficacy was maintained if patients remained in the study, which cannot be verified. Comparing the results across different studies may be difficult because of different methodologies used.

In conclusion, tofacitinib 10 mg BID had greater efficacy than 5 mg BID and efficacy was sustained for up to 2 years across the Pivotal and LTE studies in patients with moderate to severe plaque psoriasis. During the first 52 weeks, occurrence of AEs, SAEs, and discontinuations because of AEs were similar between doses. Generally, IRs for safety events were consistent between the first 52 weeks and overall tofacitinib exposure, although incidence of HZ was slightly higher in the overall exposure group. These data support the continued evaluation of tofacitinib as a potential new, long-term, oral treatment option for plaque psoriasis.

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